NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

PRELIMINARY PAPER EXPOSURE STUDY 25 SIGOURNEY STREET, HARTFORD, CT

Prepared For:

Jean Cox-Ganser, Ph.D.
Research Team Supervisor, Field Studies Branch
Centers for Disease Control (NIOSH)
1095 Willowdale Road
Mail Stop 2715B
Morgantown, WV 26505

Prepared By:

Environmental Health & Engineering, Inc.
60 Wells Avenue
Newton, MA 02459-3210
and
Division of Occupational and Environmental Medicine
University of Connecticut Health Center
Farmington, CT 06030

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LIST OF ABBREVIATIONS AND ACRONYMS

cm^3	cubic centimeter
EH&E	Environmental Health & Engineering, Inc.
GM	geometric mean
GSD	geometric standard deviation
HEPA	high efficiency particulate air
NIOSH	National Institute for Occupational Safety and Health
ppb	parts per billion
TVOC	total volatile organic compound
UCHC	University of Connecticut Health Center
VCD	vocal cord dysfunction
μm	micrometer

1.0 EXECUTIVE SUMMARY

Environmental Heath & Engineering, Inc. (EH&E) and the University of Connecticut Health Center (UCHC) are pleased to provide a summary of the preliminary paper exposure investigative work completed at 25 Sigourney Street, Hartford, Connecticut in February 2005. This preliminary investigation builds upon work in the *Back-to-Work Employee Paper Study* conducted by UCHC that identified paper that is reported by occupants to cause respiratory symptoms and skin rash. The findings of the preliminary paper exposure chamber study completed by EH&E and UCHC are described in this report.

The preliminary paper exposure study of 25 Sigourney Street included: 1) identification and collection of paper samples from three categories of case materials (specific forms selected by patients as problematic, papers from targeted boxes or cabinets, and papers from targeted storage rooms) and reference papers (paper identified by patients as causing no problem or papers in active use from units and floors that match sources of "case" paper); 2) collection of surface samples from the papers to identify morphological differences in dislogdeable materials between case and reference papers; and 3) completion of a controlled study of particle and volatile organic compound emissions from case and reference papers. Samples were collected from locations on the 6th, 17th, 18th and 19th floors.

The results of our preliminary sampling suggest that there may be differences in total particle concentrations generated from paper samples known to cause reactions and reference papers. Mean concentrations from case papers are greater than from reference papers, but the difference is not statistically significant. Paper from the 17th floor had significantly greater particle concentrations than paper from other floors, and accounted for much of the concentration differences found between case and reference paper. Paper category was found to be significantly associated with particle concentration, and the category of specific forms selected by patients as problematic had a particle mean concentration twice as high as the reference mean.

The results should be viewed with caution because of the fact that the concentrations for both case and reference papers are highly variable, with much overlap between the case

and reference concentration distributions. This indicates that if particle concentrations were the driving force behind the sensitive worker's reactions, the reference samples would cause reactions similar to reactions related to exposure to case papers. In addition, a potential source of bias may exist in the selection of case and reference paper leading to misclassification of paper.

The results from the preliminary study do not suggest that there is a difference in the types of dislodgeable materials associated with the case and reference samples. Case papers generally had higher amounts of opaques (ink, carbon, and rust) and biological materials than reference papers. The results also indicate that very little, if any, total volatile organic compounds (TVOCs) were detected from the paper samples, and that the case and reference concentrations were not different.

Based on the conclusions of the preliminary study, EH&E and UCHC recommend that a challenge study under controlled conditions with more complete characterization of the paper material may be a useful method to better understand the extent of the health effects and determine what paper materials in the state building at 25 Sigourney Street cause symptoms.

2.0 INTRODUCTION

The state building at 25 Sigourney Street has had a history of recurrent water damage, especially on the floors with terraces (17 and 19) or the floors directly below the terraces (16 and 18). During this time, many employees complained of respiratory and dermal symptoms associated with the building and some employees that were diagnosed with work-related diseases were transferred from state building at 25 Sigourney Street to other state buildings. Some employees were transferred to other floors within state building at 25 Sigourney Street. The symptoms of a number of employees that have moved have subsided.

Over the last several years, the State Department of Public Works has made numerous improvements to reduce identified risk factors, including improvements to the building envelope to prevent water intrusion and replacement of wall board, carpets and other materials previously subjected to moisture. With completion of these interventions (and others) and with improvement of the workers' symptoms while placed in other work environments, some individuals who had been restricted from the building returned to Sigourney Street. The patients continued with follow-up visits at the UCHC clinic.

Although overall symptoms improved while working in other buildings, at least nine of these workers had had recurring symptoms when handling or in the presence of certain papers originating from the state building at 25 Sigourney Street. A subset of these workers continued to experience respiratory and dermal symptoms when working on specific papers after returning to work in the state building at 25 Sigourney Street. These observations suggest ongoing effects related to use of certain paper materials. Following a sentinel model, such papers may contribute to exposures and illness among other individuals in the building as well.

Common complaints associated with papers are hoarseness and occasional chest tightness, shortness of breath and cough. Some of the occupants have developed dermatitis in addition to these respiratory symptoms. The reported symptoms may be pharyngospasm, sudden involuntary contraction of the pharynx that can happen to individuals exposed to sufficiently high levels of irritants. The upper airway symptoms are also consistent with a diagnosis of vocal cord dysfunction (VCD). Decrements in

pulmonary function have been confirmed for at least one patient that appear associated with the patient working with certain materials in the building, but not when working with a sample of other materials in the building. Direct observation of the vocal cords in a clinical setting would be required to assess a diagnosis of VCD or vocal cord inflammation.

With the advice and support of National Institute for Occupational Safety and Health (NIOSH), EH&E and the UCHC conducted a preliminary investigation of paper-related inhalation exposures in the state building at 25 Sigourney Street that was designed to characterize concentrations of particulate and TVOC arising from handling of selected papers from the building.

3.0 METHODS

3.1 PAPER SELECTION

Case papers were those identified as associated with respiratory symptoms or skin rash according to occupant interviews performed as part of the *Back-to-Work Employee Paper Study* conducted by UCHC. Case paper from specific filing cabinets, boxes, and areas of concern on specific floors were selected by UCHC for inclusion in the present study based on occupant interviews. For participants in the *Back-to-Work Employee Paper Study* unable to identify a specific location or filing cabinet as associated with papers of concern, paper commonly used as part of their daily work activities were noted and identified as case papers for the present investigation. In addition to paper from the building, several paper samples retrieved from off-site locations (92 Farmington Avenue and Rocky Hill) but handled within the state building at 25 Sigourney Street were also identified as case papers.

Case papers were selected from eleven unique locations grouped into three categories: 1) specific forms or batches of forms based on worker use and selected by patients as problematic; 2) targeted filing cabinets or boxes of concern; and 3) filing rooms of stored paper materials. Three samples of paper, each consisting of five loose sheets of paper or a single file folder, were selected from each location.

Reference paper was selected from the same floor and work unit as case paper. Reference paper was either directly identified by participants as having no association with respiratory difficulty or dermal irritation, or identified by participants as paper that had been in the building for no more than one to two years. Three samples of reference paper were collected from each of the eleven locations noted above. In summary, reference paper included copy paper, printer or fax paper, and as similar to the case paper as possible. In addition, paper that was not associated with the state agencies that occupy the state building at 25 Sigourney Street was collected off-site and included as reference paper. During the testing, the chamber operators were blinded to the case status of the sample.

3.2 EMISSION TESTING

There are no established methods available to specifically analyze paper surface emissions. Potential emissions from paper that may cause irritant or allergic symptoms include particulate matter and volatile organic compounds. Therefore a systematic approach was used to develop the testing method used in the study.

Briefly, concentrations of particulate matter and TVOC during and following manipulation of case and reference papers were determined within a glovebox. Size-fractionated particle counts within the chamber were measured with a Climet Particle Counter (Climet Instruments Company, Redwoods, California). Thirteen-second average particle counts were recorded over the duration of each trial. Ten-second average TVOC measurements were recorded with a ppbRAE Photoionization Detector (RAE Systems Inc., Sunnyvale, California).

Prior to each test, high efficiency particulate air (HEPA) filtered and activated charcoal filtered air was introduced into the chamber at a flow rate of 75 liters per minute for five minutes to achieve stable baseline values for particles and TVOCs. After achieving a stable baseline, the filtered airflow was reduced to 8.5 liters per minute. Each test was conducted for three minutes. During the first two minutes, a technician wearing gloves integral to the chamber shuffled the papers manually following a consistent routine. During the final minute of the procedure, the paper sample was placed on the floor of the chamber and not handled or manipulated.

At the conclusion of each test, the chamber was vacuumed with a HEPA equipped vacuum cleaner and all chamber surfaces were wiped with a damp, lint-free rag.

3.3 SURFACE SAMPLES

To determine the types of dislodgeable materials on the case and reference papers, a surface tape sample was collected from one sheet of paper from one-third of the samples (one sample per location) prior to the chamber sampling. Severn Trent Laboratories characterized the content of the surface samples by direct microscopic observation. Results are reported as the percentage of the surface sample identified as each of the following categories: mineral grains, opaques, synthetic fibers, biologicals,

and glass fibers. Within some of these categories, the laboratory provided an additional level of characterization, for example, opaques might include rust, metallic chips, ink, and carbon.

3.4 DATA ANALYSIS

SAS statistical software version 8.2 (SAS Institute, Inc., Cary, North Carolina) was used for all statistical analyses. The mean particle concentration over the 3-minute study period was calculated for total particles, particles less than 3.0 μm and particles greater than 10 μm for each sample. The particle data exhibited positive skewness, therefore, the data was log-transformed for purposes of data analysis and statistical inference based upon parametric techniques, including regression analysis. Non-parametric methods were also used to evaluate relationships between selected variables.

4.0 RESULTS

A total of 66 samples, 33 case samples and 33 reference samples were analyzed. Of those samples, 5 case and 5 reference samples were folders. Two of the case samples were carbonless paper samples. The folder and carbonless paper samples were excluded from most of the analyses presented here primarily because of the low sample numbers of these types. In addition to the 66 samples included in the case/reference analysis, three samples were analyzed from the UCHC offices as comparison samples.

The geometric mean (GM) total particle concentration for case paper was 174 particles per cubic centimeter (particles/cm^3), while the GM concentration for the reference papers was 139 particles/cm^3 (Table 4.1). The difference in GM particle levels between case and reference papers was not statistically significant. The GM of the UCHC samples was similar to that of the case samples, however, the maximum concentration was substantially lower than the maximum concentrations of either the case or reference samples. The GM concentration of the case folder samples was 32 particles/cm^3, and the particle concentrations generated from the two carbonless paper samples were 48 and 129 particles/cm^3, less than the GM of the reference and case papers.

Table 4.1 Descriptive Statistics for Paper Samples

Paper Status	Number of Paper Samples	Total Particles per cm^3				
		GM	GSD	Minimum	Median	Maximum
Case	26	174	2.76	19	184	1273
Reference	28	139	2.23	52	111	1160
UCHC	3	188	1.52	125	183	290

cm^3 cubic centimeter
GM geometric mean
GSD geometric standard deviation

Table 4.2 displays descriptive statistics for case and reference papers by floor of the building. Samples collected from the 17th floor had the highest GM concentrations for case (420 particles/cm^3) and reference (211 particles/cm^3) papers, as well as the greatest difference between case and reference papers. Particle concentrations from paper samples collected from the 6th, 18th and 19th floors were all approximately

100 particles/cm^3. Case papers collected from 92 Farmington and Rocky Hill had higher GM particle concentrations than any other location except the 17^{th} floor.

When analyzed by regression analysis, floor was significantly associated with total particle concentration (p-value = 0.01). When case status was included in the regression model, floor remained significantly associated with concentration, however case status was not related to concentration (p-value = 0.44). When the floor variable was dichotomized as either the 17^{th} floor or other, the samples collected from the 17^{th} floor had significantly greater particle concentrations irrespective of case status (p-value = 0.003).

Table 4.2 Descriptive Statistics by Floor

Paper Status	Floor or Location	Number of Paper Samples	Total Particles per cm^3				
			GM	GSD	Minimum	Median	Maximum
Case	6	3	103	1.18	87	103	121
Reference	6	3	98	1.41	67	104	133
Case	17	5	420	2.02	206	353	1,273
Reference	17	11	211	2.30	52	207	979
Case	18	4	107	5.79	19	222	567
Reference	18	5	96	1.16	82	93	123
Case	19	6	98	1.97	53	76	317
Reference	19	9	115	2.50	53	91	1,160
Case	92 Farmington	5	233	2.05	84	251	530
Case	Rocky Hill	3	254	2.53	101	251	645

cm^3 cubic centimeter
GM geometric mean
GSD geometric standard deviation

When analyzed by sample category, the category was associated with particle concentration (p-value=0.04). The samples of specific forms or batch of forms associated with symptoms had a GM particle concentration nearly twice as high as the reference samples (Figure 4.1).

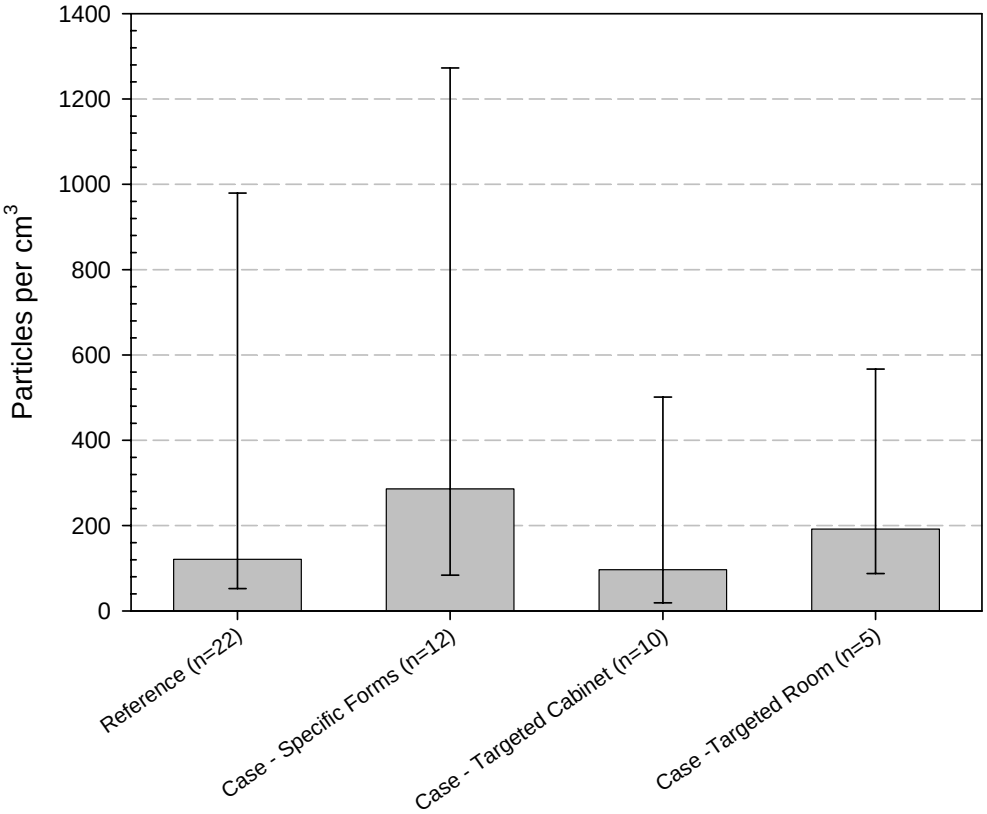

Figure 4.1 Geometric Mean Particle Concentration by Sample Category
(Error bars represent the minimum and maximums)

The GM concentrations by sampling location are graphically represented in Figure 4.2. Of the eleven case sample locations, four locations had a minimum concentration greater than the average of the reference samples. Of these four locations, three are on the 17th floor and one is on the 18th floor.

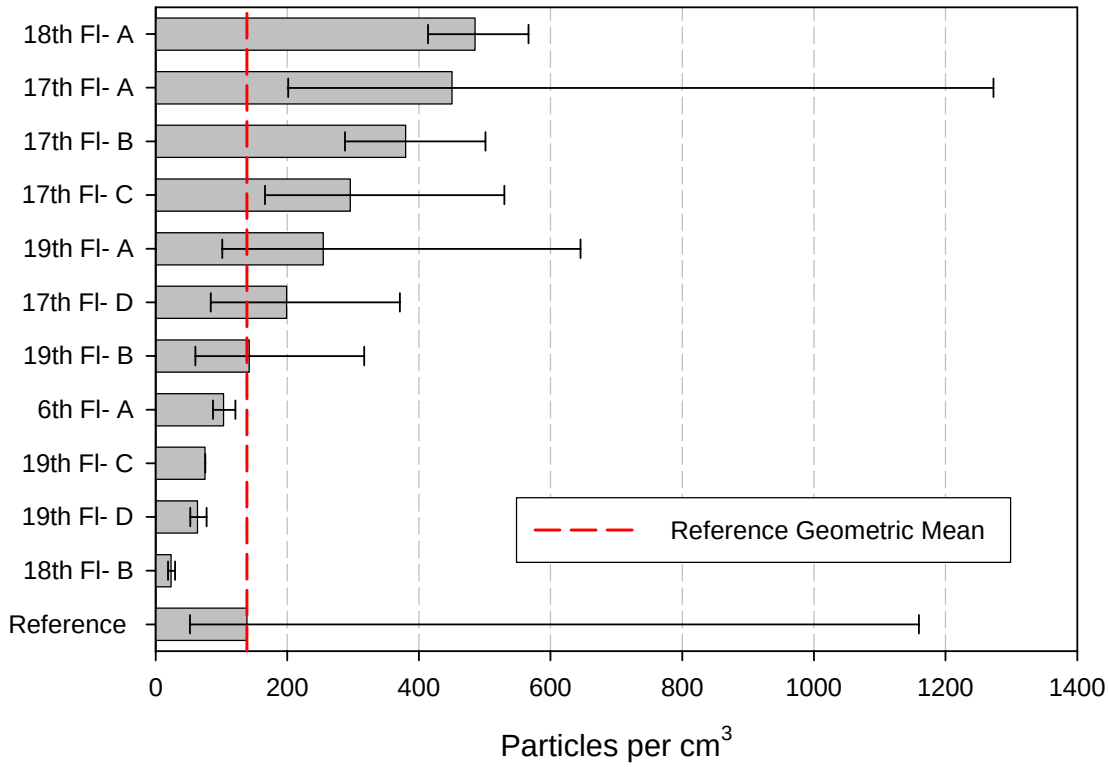

Figure 4.2 Geometric Mean Particle Concentration by Sampling Location
(Error bars represent the minimum and maximums)

To assess the affect of the age of the paper, samples were analyzed by the year of the form (Figure 4.3). From the graphical representation, age appears to have an inverse relationship with particle concentrations for case and reference papers.

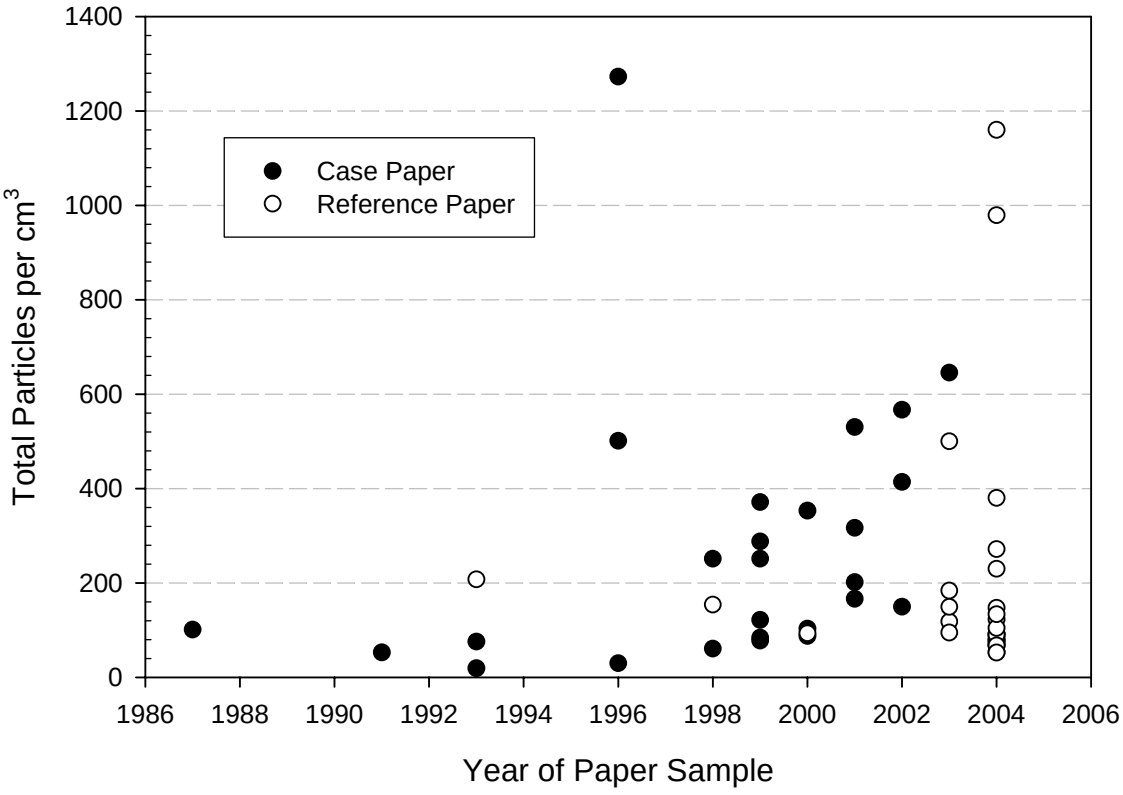

Figure 4.3 Total Particle Concentrations by Paper Age

The analyses discussed above, focused on total particle concentrations. The same analyses were also conducted on concentrations of particles less than 3.0 micrometers (μm) and particles greater than 10 μm. The results for the size-specific analyses were similar to results of the total particle concentrations. In general, the case and reference papers had similar particle size distributions (Figure 4.4).

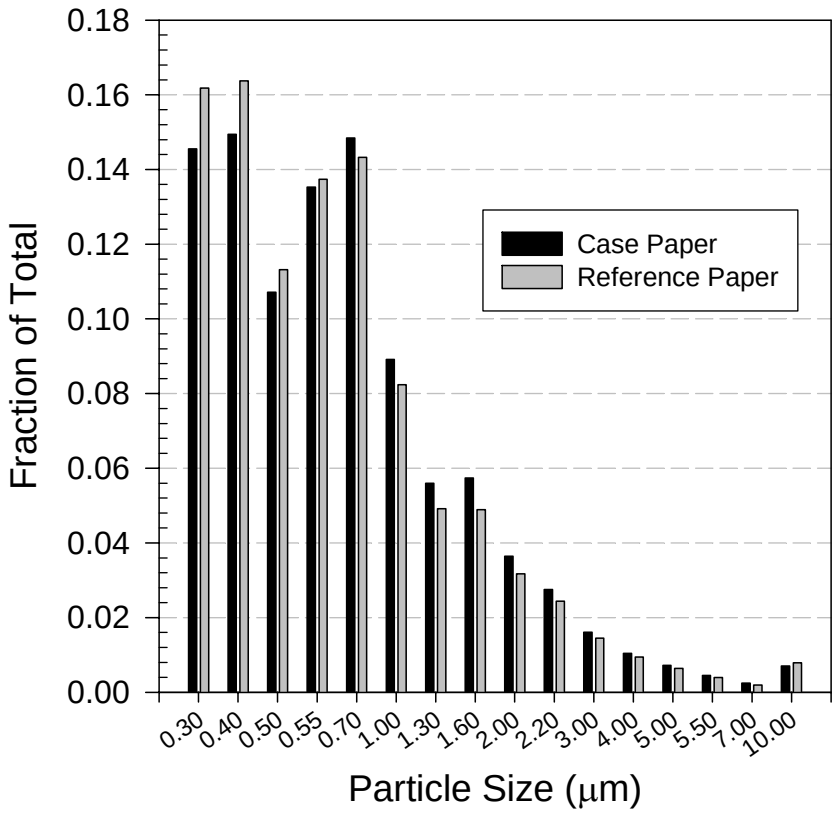

Figure 4.4 Particle Size Distributions of Case and Reference Paper

The surface sample results are reported in Table 4.3. The composition of the dislodgeable materials is reported as a percentage of the total material collected from each sample. Mineral grains, opaques and cellulose were identified in all of the samples. In general, the reference samples had higher amounts of mineral grains, while the case samples had higher amounts of opaques. Biological material was found in small amounts in both case and reference samples. On a qualitative basis the case paper reflected more biological material than reference paper. The biological material was principally identified as organic debris with only one sample having a fungal spore cluster detected. Rust or metallic chips were identified in eight of the eleven case samples and three of the eleven reference samples.

Table 4.3 Surface Composition

Material	Case (n=11)				Reference (n=11)			
	P	Mean	Min.	Max.	P	Mean	Min.	Max.
Mineral Grains	100%	29.8	2	85	100%	48.9	15	85
Opaques (ink, carbon, rust)	100%	41.2	3	90	100%	30.5	5	55
Synthetic Fiber	27%	2.1	0	15	27%	1.4	0	10
Cellulose	100%	17.7	2	65	100%	15.4	5	45
Biologicals	73%	9.0	0	30	55%	3.6	0	12
Glass Fibers	9%	0.2	0	2	9%	0.3	0	3

P percent
Min. minimum
Max. maximum

Total volatile organic compound concentrations were not significantly different between case and reference samples. The geometric mean concentration for the case paper (28.7 parts per billion [ppb]) was slightly less than the geometric mean concentration for the reference samples (29.3 ppb). The paper samples appear to have released very little volatile organic compounds as the concentrations recorded during the tests were approximately equal to concentrations observed during method blank runs within the chamber.

5.0 LIMITATIONS

A potential source of misclassification exists in selection of reference and case paper. Specific locations or cabinets that were of concern to patients were easily identified. However, it was more difficult for patients to target a specific piece of paper for either case or reference category. Without challenge testing it is difficult to be sure all reference papers selected were not eliciting symptoms. While specific reference papers were identified by patients, some of the reference papers were selected using the industrial hygienist's judgment as to papers that were similar to the case papers but not likely of concern to patients.

An additional limitation was due to the sampling methodology. The glove box was constructed of plastic, and consequently, released small quantities of TVOCs. Therefore, we were unable to determine a TVOC emission rate specific to the paper samples. The surface sample analysis was limited in several ways. First, samples were collected from only one third of the samples. Second, the surface samples only covered a small portion of the overall surface area of the paper samples. Third, it is unknown how the surface samples related to particle emissions from the paper.

6.0 CONCLUSION

Conclusions drawn from the preliminary paper characterization study include:

- Geometric mean particle concentrations are nominally greater from case papers than from reference papers, but the difference is not statistically significant based on the sample size of 26 pairs of case and reference paper.

- The distribution of particle concentrations from case and reference papers was approximately equal.

- Papers obtained from the 17th floor of the state building at 25 Sigourney Street accounted for much of the differences observed in particle concentrations between case and reference papers.

- Particle concentrations are inversely related with age of the paper, a finding that is opposite of our *a priori* hypothesis that older paper would produce greater concentrations of particles due perhaps to settling of dust on the paper and the degradation of the paper.

- Tape lift samples from case paper had nominally greater amounts of opaques (ink, carbon, rust) and biological material (principally organic debris) than tape lift samples from reference paper.

- Few, if any, volatile organic compounds were detected by case and reference papers.

7.0 RECOMMENDATIONS

EH&E and UCHC recommend that a challenge study under controlled conditions may be a useful method to determine if the specific case papers cause a reaction outside of the state building at 25 Sigourney Street. This study would include exposing sensitive and non-sensitive individuals to paper samples in a blinded way to both case papers (specific forms thought to cause reactions) and reference papers. This study would likely need to be conducted in a hospital setting for safety. Investigators may consider a two-by-two design that includes challenging paper-related patients seen by UCHC clinicians and controls with case and reference paper from the state building at 25 Sigourney Street and possibly other locations. A study of this type has many desirable features.

A challenge study would evaluate the impact of paper products or contaminants on patients identified with complaints they attribute to paper and non-symptomatic control subject. The study would eliminate the confounding factor of working in a building where occupants continue to note symptoms that may not be related to paper. Outcomes that could be directly observed include: skin eruptions, laryngeal swelling or spasm, and spirometric changes. If no different responses were documented, this would provide important evidence that paper is not causing ongoing symptoms in the building. This result would have important ramifications for further remediation efforts for this workforce. Finally, concerns regarding paper products and contaminants have been raised in other indoor settings. Little information is available to guide clinical evaluation, exposure evaluation, or intervention in those settings. This investigation could provide important information of consequence beyond this particular building.